Biotinidase Deficiency Fact Sheet

Biotinidase Deficiency

Biotinidase deficiency is an autosomal recessive metabolic disorder affecting biotin (a B-complex vitamin) recycling. Individuals with biotinidase deficiency do not have enough of the enzyme biotinidase required to recycle endogenous biotin and release dietary protein-bound biotin. This leads to deficiency of multiple carboxylases involved in the metabolism of amino acids and carbohydrates. There may be a profound deficiency or partial deficiency.

Types of Deficiency

Profound deficiency: Individuals with this type of deficiency have no activity or less than or equal to 10% normal biotinidase activity in the serum. Left untreated, symptoms include seizures, hypotonia, skin rash and/or alopecia, developmental delay, conjunctivitis, visual problems such as optic atrophy, sensorineural hearing deficit, metabolic acidosis with elevation of both lactate and ketones, and organic acidemia. With treatment, the most rapid improvement occurs for organic acidemia, skin rash, muscle tone, and seizures. Hair begins to grow back within weeks to months. Profound biotinidase deficiency occurs in about 1 in 38,000 births per year. It is anticipated that approximately 13 newborns with profound biotinidase deficiency will be identified by the California Newborn Screening Program each year.

Partial Deficiency: Individuals with this deficiency have between 10-30% normal biotinidase activity in their serum. They are often asymptomatic but may develop the same neurologic and cutaneous symptoms as profound biotinidase deficiency at times of stress such as an illness or poor diet. Partial biotinidase deficiency occurs in about 1 in 140,000 births per year. Approximately 4 newborns with partial biotinidase deficiency will be identified by the California Newborn Screening Program each year. The Newborn Screening Program will only identify some of these newborns.

Treatment

Biotinidase deficiency is not a life-threatening disease with proper treatment. Biotin supplement begins shortly after birth. Over-the-counter biotin products and health supplements do not have the appropriate doses. The recommended daily dose is between 5-20 mg per day. However, this needs to be determined in consultation with a metabolic specialist. Treatment is life-long. The biotin supplement can be given by either capsule or tablet. Pharmacies can make liquid preparations for babies and children. However, there are potential problems with liquid forms such as settling out which can lead to inadequate dosing, additionally this form is prone to bacterial growth. Infants treated before symptoms appear usually do not develop any symptoms of biotinidase deficiency. Occasionally missing a dose probably will not harm an individual with biotinidase deficiency but if medication or administration is inconsistent, symptoms of

biotinidase deficiency may appear. If at any time the child develops any symptoms of biotinidase deficiency, the child needs to be examined to determine the proper dose of biotin.

The California Newborn Screening Program

A legislative mandate required that the California Newborn Screening Program add biotinidase deficiency to the newborn screening panel starting July 2007. The newborn screening uses a small amount of blood obtained from a heel-stick for a colorimetric test for biotinidase activity. If this initial test is positive, the Newborn Screening Area Service Center staff arrange for the collection of another blood spot, i.e., repeat test specimen, through the infant's primary care physician. A confirmatory test which measures biotinidase activity in serum/plasma is warranted if the initial test is below a certain cut off level or if the repeat test is positive. All newborns screened through the California Newborn Screening Program with an initial result of > 10 ERU will be considered negative. Initial positive result for biotinidase deficiency with values between 6.01-10.00 ERU will have a repeat test in which if the result is greater than 10 ERU the result is negative and no follow-up is needed. For repeat test results < 10 ERU, the newborn will be referred to Stanford for confirmatory testing. For initial positive results ≤6 ERU, the newborn will be automatically referred to a Stanford for confirmatory testing and a CCS-approved metabolic center for diagnostic evaluation and development of treatment plan when indicated.

Preliminary results of California's Newborn Screening Program for biotinidase deficiency (BD) from July 15, 2007 through April 15, 2008, indicated a much higher prevalence of screened positive BD cases than expected. Among 429,243 newborns screened during this time period, 10 infants with profound BD have been identified with an incidence rate of 1 per 38,461 and 3 infants identified with partial BD with an incidence rate of 1 per 142,857. The total BD incidence rate was 1 per 33,333. California's rates for profound and total BD are higher than the worldwide rates reported previously.